

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

To:

DORSEY & WHITNEY LLP  
Attn. Abelev, Gary  
250 Park Avenue  
New York NY 10177  
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

Patent Mail Received

AUG 12 2008

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

07/08/2008

Applicant's or agent's file reference

187296/PCT

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/US2007/074873

International filing date  
(day/month/year)

31/07/2007

Applicant

THE GENERAL HOSPITAL CORPORATION

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 338.82.70

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the international Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of **18 months** from the priority date, the International application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
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Authorized officer

Ka-Bo Müller

**DOCKETED**

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

**The amendments must be made in the language in which the international application is to be published.**

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 187296/PCT	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2007/074873	International filing date (day/month/year) 31/07/2007	(Earliest) Priority Date (day/month/year) 01/08/2006
Applicant THE GENERAL HOSPITAL CORPORATION		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

- b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6(b)(a)).  
 c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant  
☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 6

☒ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention

- b. ☐ none of the figures is to be published with the abstract

**Box No. IV    Text of the abstract (Continuation of item 5 of the first sheet)**

An optical fibre arrangement for Raman Spectroscopy wherein at least one portion of the fiber arrangement may be composed of or can include therein sapphire, diamond, clear graphite, Chalcogenide, borosilicate, zirconium fluoride, silver halide, a liquid core light guide, a gas core light guide, a hollow core waveguide, and/or a solid core photonic crystal fiber. A receiving arrangement may be configured to receive the electromagnetic radiation that is filtered and received from the sample. At least one first characteristic of at least one portion of the optical fiber can be controlled so as to modify at least one second characteristic of at least one second electromagnetic radiation generated within the optical fiber. The second electromagnetic radiation can be associated with the first electromagnetic radiation.

A. CLASSIFICATION OF SUBJECT MATTER  
INV. G01J3/44 G01N21/65

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B G01J G01N G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SHIM M G ET AL: "STUDY OF FIBER-OPTIC PROBES FOR IN VIVO MEDICAL RAMAN SPECTROSCOPY" APPLIED SPECTROSCOPY, THE SOCIETY FOR APPLIED SPECTROSCOPY. BALTIMORE, US, vol. 53, no. 6, June 1999 (1999-06), pages 619-627, XP000827480 ISSN: 0003-7028 cited in the application the whole document	1-12,42
X	US 2004/263843 A1 (KNOPP KEVIN J [US] ET AL) 30 December 2004 (2004-12-30) paragraph [0030] ----- -/--	1,5,6, 10,42

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

9 April 2008

Date of mailing of the international search report

07/08/2008

Name and mailing address of the ISA/  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax. (+31-70) 340-3016

Authorized officer

Croucher, J

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BINDIG U ET AL: "Fibre-optic laser-assisted infrared tumour diagnostics (FLAIR); Infrared tumour diagnostics" JOURNAL OF PHYSICS D. APPLIED PHYSICS, INSTITUTE OF PHYSICS PUBLISHING, BRISTOL, GB, vol. 38, no. 15, 7 August 2005 (2005-08-07), pages 2716-2731, XP020083258 ISSN: 0022-3727 page 2718 - page 2719 -----	1,2,5-8, 10-12,42
A	WO 98/00057 A (UNIV TEXAS [US]; MAHADEVAN JANSEN ANITA [US]; RICHARDS KORTUM REBECCA) 8 January 1998 (1998-01-08) page 9, line 20 - page 11, line 23 -----	1-12,42

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/074873

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-12, 42

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

## 1. claims: 1-12,42

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein at least one portion of the fibre is composed of or includes therein at least one of sapphire, diamond, clear graphite, Chalcogenide, borosilicate, zirconium fluoride, silver halide, a liquid core light guide, a gas core light guide, a hollow core waveguide, or a solid core photonic crystal fibre; and
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

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## 2. claims: 13-17,41

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein the at least one optical fibre is able to filter light; and
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

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## 3. claims: 18-20

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein said light is able to reduce fluorescence from said sample;
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

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## 4. claims: 21-27

A system comprising;

- at least one optical fibre for forwarding light to a sample and receive light from the sample, wherein said received light is time gated.

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## 5. claims: 28-40

A system comprising:

- at least one optical fibre for forwarding light to a sample;
- characteristic controlling means to control the temperature of at least a portion of the optical fibre so as to modify the light generated within the optical fibre.

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Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 2004263843	A1	30-12-2004	NONE		
WO 9800057	A	08-01-1998	AU	3495797 A	21-01-1998
			US	5842995 A	01-12-1998

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2007/074873

International filing date (day/month/year)  
31.07.2007

Priority date (day/month/year)  
01.08.2006

International Patent Classification (IPC) or both national classification and IPC  
INV. G01J3/44 G01N21/65

Applicant  
THE GENERAL HOSPITAL CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Date of completion of  
this opinion

see form  
PCT/ISA/210

Authorized Officer

Croucher, J

Telephone No. +49 89 2399-2704



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US2007/074873

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 13-41

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 13-41

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

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**Box No. IV Lack of unity of invention**

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1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-12, 42

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	=
	No: Claims	<u>1-12, 42</u>
Inventive step (IS)	Yes: Claims	=
	No: Claims	<u>1-12, 42</u>
Industrial applicability (IA)	Yes: Claims	=
	No: Claims	=

2. Citations and explanations

see separate sheet

**Section IV: Lack of unity of invention**

- 1.1 This International Search Authority found five inventions in this international application, as follows, with paraphrasing for reasons of clarity:

*Invention 1 - Claims 1-12 and 42:*

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein at least one portion of the fibre is composed of or includes therein at least one of sapphire, diamond, clear graphite, Chalcogenide, borosilicate, zirconium fluoride, silver halide, a liquid core light guide, a gas core light guide, a hollow core waveguide, or a solid core photonic crystal fibre; and
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

*Invention 2 - Claims 13-17 and 41:*

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein the at least one optical fibre is able to filter light; and
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

*Invention 3 - Claims 18-20:*

A system comprising:

- at least one optical fibre for forwarding light to a sample, wherein said light is able to reduce fluorescence from said sample;
- at least one receiving arrangement to receive light filtered and received from the at least one sample.

*Invention 4 - Claims 21-27:*

A system comprising;

- at least one optical fibre for forwarding light to a sample and receive light from the sample, wherein said received light is time gated.

*Invention 5 - Claims 28-40:*

A system comprising:

- at least one optical fibre for forwarding light to a sample;
- characteristic controlling means to control the temperature of at least a portion of the optical fibre so as to modify the light generated within the optical fibre.

- 1.2 The requirement of Rule 13.1 PCT implies that if an invention is to be defined by a plurality of independent Claims, then these Claims should be linked together by a common concept which must be new and inventive. However, the only feature common to all the independent Claims is the excitation optical fibre for transmitting light to the sample, which is commonly known. For this reason it is considered that the Claims on file can be divided into five inventions.
- 1.3 The present application is thus related in a first aspect (Claims 1-12 and 42) to an optical probe comprising a special optical fibre.
- 1.4 The application is related in a second aspect (Claims 13-17 and 41) to a system for transmitting filtered light to and from a sample through optical fibres.
- 1.5 The application is related in a third aspect (Claims 18-20) to using photo-bleaching to reduce sample autofluorescence.
- 1.6 The application is related in a fourth aspect (Claims 21-27) to using time resolution to reduce the collection of fluorescent signals from the sample.
- 1.7 The application is related in a fifth aspect (Claims 28-40) to controlling the temperature of an optical probe in order to protect the environment surrounding the optical fibre. Although temperature is not specifically mentioned in independent

Claims 28, 39 and 40 this is the only "characteristic" disclosed in the description.

- 1.8 Thus, the application does not meet the requirements of unity of invention as defined by Rule 13.1 and 13.2 PCT.

## Section V: Novelty, inventive step and industrial applicability

### Invention 1: Claims 1-12 and 42

#### 2 Prior art

- 2.1 Reference is made to the following documents:

- D1 SHIM, M G, et al. Study of fiber-optic probes for *in vivo* medical Raman spectroscopy. Applied Spectroscopy. 1999. Vol. 53, Nr. 6, pages 619-627; XP000827480.
- D2 US 2004/0263843 A1 (KNOPP)
- D3 BINDIG, U and MÜLLER, G. Fibre-optic laser-assisted infrared tumour diagnostics (FLAIR); Infrared tumour diagnostics. Applied Physics. 2005. Vol. 38, Nr. 15, pages 2716-2731; XP020083258.
- D4 WO 98/00057 A1 (BOARD OR REGENTS)

#### 3 Novelty - Article 33(2) PCT

- 3.1 The present application does not meet the requirements of Article 33(1) PCT, because the subject-matter of Claims 1-12 and 42 is not new in the sense of Article 33(2) PCT.
- 3.2 Document D1 discloses (the figures in parentheses applying to this document):

A system, comprising:

- at least one fibre arrangement ("fiber-optic based Raman system"; abstract) including optical transmitting characteristics, configured to transmit therethrough at least one electromagnetic radiation and



forward the at least one electromagnetic radiation to at least one sample ("rabbit tissues"; abstract), wherein at least one portion of the at least one fibre arrangement is composed of or includes therein at least one of sapphire ("sapphire fiber"; page 622 column 1), diamond, clear graphite, Chalcogenide, borosilicate, zirconium fluoride, silver halide, a liquid core light guide ("NIR-enhanced liquid lightguides"; page 622 column 1), a gas core light guide, a hollow core waveguide, or a solid core photonic crystal fibre, and

- at least one receiving arrangement ("collection fiber probe"; page 622 column 2) configured to receive the electromagnetic radiation that is filtered ("external filters"; page 622 column 2) and received from the at least one sample.

3.3 The subject-matter of independent Claim 1, as well as independent Claims 11 and 42, *mutatis mutandis*, is therefore not new (Article 33(2) PCT).

3.4 D1 only describes in depth Raman probes comprising low-OH fibres, as liquid lightguides and sapphire fibres were rejected as unsuitable. However, it appears from D1 that these special fibres were at the very least considered. As a consequence, even if a lack of novelty (Article 33(2) PCT) is disputed the invention as claimed fails to satisfy the requirement of inventiveness (Article 33(3) PCT).

3.5 Document D1 also discloses that:

- the at least one fibre arrangement includes therein at least one filtering arrangement ("a bandpass filter was incorporated within the delivery fiber"; page 622 column 2);
- the at least one receiving arrangement includes therein at least one further filtering arrangement ("long-pass filters were used within the collection fibers"; page 624 column 1);
- the at least one receiving arrangement is at least one further fibre arrangement (figure 3);
- the received at least one electromagnetic radiation is a Raman radiation ("ex vivo spectra of rabbit tissues"; figure 12);

- a further arrangement is configured to house therein at least one portion of the at least one fibre arrangement ("micro-tubing"; figure 3);
- the sample is provided at least partly within an anatomical structure ("rabbit tissues"; figure 12);
- the at least one receiving arrangement includes a fibre arrangement which is composed of or includes therein at least one of sapphire ("sapphire fiber"; page 622 column 1), diamond, clear graphite, Chalcogenide, borosilicate, zirconium fluoride, silver halide, a liquid core light guide ("NIR-enhanced liquid lightguides"; page 622 column 1), a gas core light guide, a hollow core waveguide, or a solid core photonic crystal fibre.
- the at least one fibre arrangement includes at least one fibre which has at least one first filtering characteristic that filter the electromagnetic radiation (figure 3);
- the at least one fibre arrangement and the at least one receiving arrangement are the same (figure 3).

- 3.6 The subject-matter of dependent Claims 2-10 and 12 is therefore also not new.
- 3.7 Document D2 discloses (paragraph [0030]) the technical features of Claims 1, 5, 6, 10 and 42, using a solid core photonic crystal light guide to conduct light to the sample.
- 3.8 Document D3 discloses (page 2718 - page 2719) the technical features of Claims 1, 2, 5-8, 10-12 and 42, and describes using silver halide, chalcogenide and hollow fibres.

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	<p>In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/ WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT).</p> <p>If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).</p>
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003